

06/02/03

Reply to Office Action of December 2, 2002

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

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1. (Currently amended) A method of treating an implantable biological tissue, said method comprising stabilizing glycosaminoglycans on the tissue and cross-linking proteins on the tissue, wherein the stabilization of glycosaminoglycans on the tissue comprises contacting the tissue with a water-soluble carbodiimide composition having a pH of about 6.9 to 7.9.

2. (Original) The method of claim 1, wherein said glycosaminoglycans are endogenous to the tissue.

3. (Original) The method of claim 2, wherein the tissue is a part of an implantable bioprosthetic device.

3.
4. (Original) The method of claim 3, wherein said device is selected from the group consisting of a heart valve prosthesis, a vascular graft, a skin graft, a dura mater graft, a cartilage graft, a cartilage implant, a pericardium graft, a urinary bladder prosthesis, a ligament prosthesis, and a tendon prosthesis.

5. (Original) The method of claim 4, wherein said device is a heart valve prosthesis.

6. (Original) The method of claim 5, wherein said heart valve prosthesis is selected from the group consisting of a porcine heart valve and a bovine pericardium-derived

heart valve prosthesis.

7. (Cancelled) The method of claim 1, wherein stabilization of glycosaminoglycans on the tissue is achieved by contacting the tissue with a water-soluble carbodiimide.

8. (Cancelled) The method of claim 7, wherein cross-linking proteins on the tissue is achieved by contacting the tissue with a second carbodiimide.

9. (Cancelled) The method of claim 7, wherein cross-linking proteins on the tissue is achieved by contacting the tissue with a protein cross-linking agent other than a carbodiimide.

10. (Currently amended) The method of claim 7, wherein stabilization of glycosaminoglycans on the tissue is achieved prior to cross-linking proteins on the tissue.

11. (Original) The method of claim 10, wherein

a) the difference between i) the thermal shrinkage temperature of the tissue after contacting the tissue with said carbodiimide and ii) the thermal shrinkage temperature of the tissue prior to contacting the tissue with said carbodiimide is less than half of

b) the difference between i) the thermal shrinkage temperature of the tissue after cross-linking proteins on the tissue and ii) the thermal shrinkage temperature of the tissue prior to cross-linking proteins on the tissue.

12. (Currently amended) The method of claim ~~7~~ 1, wherein said carbodiimide is 1-ethyl-3-(3-dimethyl aminopropyl) carbodiimide.

13. (Cancelled) The method of claim 7, wherein the tissue is contacted with

said carbodiimide in an aqueous liquid having a pH of about 6.9 to 7.9.

14. (Currently amended) A method of treating an implantable biological tissue, said method comprising ~~The method of claim 1, wherein stabilization of glycosaminoglycans on the tissue is achieved by contacting the tissue with a carbohydrate oxidizing agent to generate aldehyde groups on said glycosaminoglycans on the tissue to stabilize the glycosaminoglycans, and cross-linking proteins on the tissue by contacting the tissue with a bi-functional carbohydrate-protein linking agent.~~

15. (Original) The method of claim 14, wherein said carbohydrate oxidizing agent is selected from the group consisting of bromine, periodate, nitric acid, and lead tetraacetate.

16. (Original) The method of claim 14, wherein said bi-functional aldehyde-protein linker is selected from the group consisting of glutaraldehyde, a diamine, and an azido hydrazide.

17. (Currently amended) A method of treating an implantable biological tissue, said method comprising ~~The method of claim 1, wherein stabilization of stabilizing glycosaminoglycans on the tissue is achieved by contacting the tissue with a heterofunctional azide reagent.~~

18. (Original) The method of claim 17, further comprising contacting the tissue with an agent for linking said heterofunctional azide reagent and extracellular protein or glycosaminoglycan in the tissue.

19. (Original) The method of claim 18, wherein said agent for linking said

heterofunctional azide reagent and extracellular protein in the tissue is selected from the group consisting of a dithiol, dithiothreitol, a di-aldehyde, glutaraldehyde, a di-carbonyl compound, a carbodiimide, and an epoxide.

26. (New) The method of claim 1, wherein the cross-linking comprises contacting the tissue with glutaraldehyde.

27. (New) The method of claim 1, wherein the cross-linking comprises contacting the tissue with glutaraldehyde, provided that the cross-linking is performed after the stabilizing of glycosaminoglycans.
